## Citation:

Reynolds K, Chin A, Lees KA, Nguyen A, Bujnowski D, He J. A meta-analysis of the effect of soy protein supplementation on serum lipids. Am J Cardiol. 2006;98(5):633-40

**PubMed ID:** 16923451

## Study Design:

Meta- analysis

## Class:

M - Click here for explanation of classification scheme.

## Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

## Research Purpose:

To examine the effect of soy protein supplementation on serum lipid levels by pooling the results from randomized controlled trials of isolated soy protein supplementation.

## Inclusion Criteria:

- Each study had to:
- be a randomized controlled trial;
- conducted in adults ( i.e., ≥ 18 years of age);
- use concurrent control groups;
- have limited intervention differences between groups to soy protein supplementation in the form of isolated soy protein;
- report changes in serum lipids (triglycerides, total, LDL, and/or HDL cholesterol) from baseline to follow-up and the corresponding variances or sufficient data to estimate them.
- use human subjects

## Exclusion Criteria:

- Non randomization of the trial participants.
- Study design other than controlled clinical trial.
- Lack of an appropriate concurrent control group.
- Participants <18 years of age.
- Lack of data on serum lipids outcome.
- Use of soy-based supplements other than isolated soy protein.
- Full length text not available. Same trial participants as in trials already included.
- When ≥ publications were based on the same study, the report with the largest number of participants was selected.

## Description of Study Protocol:

### Recruitment

- A comprehensive, systematic search of published reports was conducted using the MEDLINE database ( 1966 to February 2005) and the following medical subject headings: lipids, lipoproteins, LDL- cholesterol, HDL-C, VLDLD-C, cholesterol, soybean proteins, soybeans and isoflavones.

### Design

- English language articles were retrieved by searching of 41 randomized controlled trials in which isolated soy protein supplementation was the only intervention and the net changes in serum lipids during intervention were reported.
- The search was restricted to studies published in English-language journals and conducted in human subjects.
- Information on study design, sample size, participant characteristics, intervention, follow-up-duration and treatment outcomes was independently abstracted using a standardized protocol. Using a random-effects model, data from each study were pooled and weighted by the inverse of their variance.

### Blinding used (if applicable)

N/A

### Intervention (if applicable)

- Isolated soy protein supplementation

### Statistical Analysis

- The mean baseline cholesterol and triglyceride values for each trial were calculated by combining the mean values from the intervention and control groups, weighted by the number of subjects. For parallel and factorial trials, the net changes were calculated by the difference (intervention minus control) of the changes (baseline minus follow-up) of the mean values. For cross-over trials the net changes were calculated as the mean difference of values at the end of the intervention and control periods.
- To pool the overall effect size, each study was weighted by the reciprocal of the total variance for change in serum cholesterol (separate values for total, LDL, HDL cholesterol) and triglyceride levels. The variances for net changes were calculated using CIs, p values, t statistics or individual variances for intervention and control groups (parallel and factorial design) or intervention and control periods (crossover design) .
- For parallel trials that reported the variance for paired differences separately for each group, standard methods were used to calculate the pooled variance for the net change.
- Fixed effects and DerSimonian and Laird random effects models were used to calculate the pooled estimated mean effect of soy protein supplementation on the cholesterol and triglyceride levels.
- A sensitivity analysis was conducted to examine the influence of various exclusion criteria on the overall effect sizes.
- Statistical significance for each subgroup was tested using one way analysis of variance, weighted by the inverse of the total variance for the change in serum lipids.
- Meta-regression analysis with no intercept term was performed to examine the dose-response relation between soy protein or isoflavones and the net change in lipids, weighting by the inverse of the variance.

## Data Collection Summary:

### Timing of Measurements

The studies were conducted from 1982 to 2004 .

Duration of the intervention range in the studies: 3 to 52 wks.

### Dependent Variables

- Net change in total cholesterol, HDL cholesterol and LDL cholesterol

### Independent Variables

- soy protein intake, isoflavone inake

### Control Variables

## Description of Actual Data Sample:

**Initial N**:

N=147 abstract or reports identified

**Attrition (final N)**: N=27 included in meta-analysis (totaling 41 comparisons, and including 1756 participants)

**Age**: Mean range : 22-67 years

**Ethnicity**: NA

**Other relevant demographics**: Age, gender, soy intake ranged from 20 to >61 g/d, isoflavone intake ranged from 2 to 192 mg/d, The average pretreatment lipid levels varied from 129 to 293 mg/dL for total cholesterol, 75 to 198 mg/dL for LDL cholesterol, 37 to 61 mg/dL for HDL cholesterol and 53 to 204 mg/dL for triglycerides.

**Anthropometrics** NA

**Location**: USA, Canada, Norway, Italy, Australia, Japan, UK, Finland, Israel, Chile, The Netherlands

## Summary of Results:

- The studies were conducted from 1982 to 2004 and varied in sample size from 4 to 179 participants (median 37). The amount of isolated soy protein consumed during the interventions ranged from 20 to >61 g/d.The amount of isoflavones used in the studies ranged from 2 to 192 mg/d. 41 trials were reported in this study. 27 were conducted in the United States.
- Overall, 1756 participants were evaluated. All trials were conducted in adults. Mean age range : 22 to 67 years.18 trials reported in women of which 12 were conducted among postmenopausal women.8 consisted entirely of men and 11 consisted of men and women. 31 trials reported on the hypercholesterolemic status.19 trials in participants with hyperlipidemia. 9 were conducted in participants with normal lipid levels and 3 trials included participants with and without hyperlipidemia. The trials varied in length from 3 to 52 weeks.
- Soy protein supplementation was association with a significant reduction in mean serum total cholesterol (-5.26 mg/dL, 95% CI: -7.14 to -3.38), low density lipoprotein cholesterol (-4.25 mg/dL, 95%CI: -6.00 to -2.50) and triglycerides (-6.26 mg/dL, -6.26 to 3.38) and a significant increase in high-density lipoprotein cholesterol (0.77 mg/dL, 95%CI: 0.20 to 1.34). Meta regression analyses showed a dose response relation between soy protein and isoflavone supplementation and net changes in serum lipids. These results indicate that soy protein supplementation reduces serum lipids among adults with or without hypercholesterolemia.
- Total cholesterol decreased in 30 of the 41 trials, but the reduction was statistically significant in only 7.
  LDL cholesterol and triglycerides decreased in 28 of the 38 trials and 27 of the 39 trials, respectively, but the reductions were statistically significant in only 7 and 5 trials respectively.
  HDL cholesterol increased in 25 of the 38 trials, but the increase was statistically significant in only 2 trials.
- Statistically significant inverse relations were found between the amount of soy protein and isoflavones and the net changes in total cholesterol, LDL cholesterol and triglycerides and positive relations were found between amount of soy protein and isoflavones and the net changes in HDL cholesterol.
- A crossover design was used in 20 trials, a Latin-square design in 4 trials, a parallel design in 17 trials, and a factorial design in 2 trials. Of the 29 trials that reported their methods of blinding, 25 were double blind, 2 were single blind and 2 were open labeled. The average pretreatment lipid levels varied from 129 to 293 mg/dL for total cholesterol, 75 to 198 mg/dL for LDL cholesterol, 37 to 61 mg/dL for HDL cholesterol and 53 to 204 mg/dL for triglycerides.
- The effect size of soy protein supplementation on total and LDL cholesterol was slightly greater in participants with a mean baseline total cholesterol level of <240 mg/dL and LDL cholesterol level of <160 mg/dL compared with those with elevated cholesterol levels (total cholesterol ≥ 240 mg/dL or LDL cholesterol ≥160 mg/dL) and among pre and/or peri-menopausal women compared with post-menopausal women.
- The effect of soy protein supplementation on HDL cholesterol was slightly greater in participants with elevated total cholesterol levels at baseline (total cholesterol ≥ 240 mg/dL) compared with participants with total cholesterol levels <240 mg/dL.
- The effect of soy protein supplementation on HDL cholesterol was greater among trials with a parallel design and longer intervention duration. In addition, the effect of soy protein on HDL cholesterol was significantly greater statistically among trials with a larger sample size, parallel design and longer intervention duration.
- No evidence of publication bias as indicated by the funnel plots and the Begg rank correlation test (p=0.68, p=0.31,p=0.93, and p=0.54 for total, LDL and HDL cholesterol and triglycerides, respectively).

## Author Conclusion:

- Soy protein should be an important component of a comprehensive dietary intervention for the prevention and treatment of hypercholesterolemia.
- The results suggest that soy protein supplementation lowers total cholesterol, LDL cholesterol and triglycerides and slightly increases HDL cholesterol.
- Authors conclude that replacing foods high in saturated fat, trans-saturated fat and cholesterol with soy protein may have a beneficial effect on coronary risk factors.

## *Reviewer Comments:*

- *This is a very well designed meta- analysis. Authors reported the limitations for the analysis.*

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***Research Design and Implementation Criteria Checklist: Review Articles***

## Relevance Questions

1. Will the answer if true, have a direct bearing on the health of patients? Yes

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| 2. | Is the outcome or topic something that patients/clients/population groups would care about? | Yes |
| 3. | Is the problem addressed in the review one that is relevant to nutrition or dietetics practice? | Yes |
| 4. | Will the information, if true, require a change in practice? | Yes |

**Validity Questions**

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|---|---|---|
| 1. | Was the question for the review clearly focused and appropriate? | Yes |
| 2. | Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described? | Yes |
| 3. | Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased? | Yes |
| 4. | Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible? | Yes |
| 5. | Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined? | Yes |
| 6. | Was the outcome of interest clearly indicated? Were other potential harms and benefits considered? | Yes |
| 7. | Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described? | Yes |
| 8. | Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included? | Yes |
| 9. | Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed? | Yes |
| 10. | Was bias due to the review's funding or sponsorship unlikely? | Yes |